REMARKS/ARGUMENTS

Status of the Claims

In response to the Restriction Requirement mailed June 1, 2006, Applicants previously elected to prosecute the claims of Group I, namely claims 1-3, 7, and 9-15. The Examiner has now indicated that claim 7 has been removed from Group I and has been placed in new Group VI. Applicants confirm the election of Group I (presently claims 1-3 and 9-15) and expressly reserve the right to file divisional applications or take such other appropriate measures deemed necessary to protect the invention of claim 7.

Claims 1-3 and 9-15 were rejected. Claims 4-8 and 16-20 were withdrawn from consideration as being drawn to nonelected inventions and have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue these claims in a continuation or divisional application or to take other such appropriate action to seek protection of this canceled subject matter.

Claims 1 and 13 have been amended to expedite prosecution. Support for these amendments can be found in the specification and in the specification and originally filed claims. No new matter has been added by way of these amendments. Claims 1-3 and 9-15 are now pending in the present application. Reexamination and reconsideration of these claims are respectfully requested in view of the claim amendments and the following remarks. The Examiner's comments in the Office Action are addressed below in the order set forth therein.

The Objection to Figure 2 Should Be Withdrawn

The Examiner has objected to Figure 2 that was submitted on March 11, 2004 as part of the originally filed application because the highlighted portions of the figure are too dark to be legible. The shaded portions of Figure 2 have been lightened to address this issue. A substitute Figure 2 is submitted herewith. Accordingly, in light of the amendment of Figure 2, the Examiner's objection has been obviated and should be withdrawn.

The Objection to the Specification Should Be Withdrawn

The specification was objected to for use of the trademark name "Gibco." The specification has been amended such that each reference to "Gibco" is capitalized and followed by a proper trademark symbol (i.e., GIBCO™), as required by MPEP 608.01(v). In light of the amendments to the specification, the objection has been obviated and should be withdrawn.

The Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 1-3 and 9-15 were rejected under 35 U.S.C. § 112, first paragraph, as failing to satisfy the written description requirement. This rejection is respectfully traversed.

Original claims 1-3 are directed to an isolated nucleic acid molecule selected from the group consisting of the nucleotide sequence set forth in SEQ ID NO:1, a nucleotide sequence encoding the amino acid sequence set forth in SEQ ID NO:2, a nucleotide sequence having at least about 90% or about 95% sequence identity to the nucleotide sequence of SEQ ID NO:1, wherein the nucleotide sequence encodes a polypeptide having *Bacillus thuringiensis* (*Bt*) toxin binding activity, a nucleotide sequence that hybridizes to the complement of the nucleotide sequence of SEQ ID NO:1 under stringent conditions, the nucleotide sequence of the cDNA insert of the plasmid deposited with the ATCC as Patent Deposit No. PTA-4935, and a nucleotide sequence complementary to at least one of the above-referenced sequences. Claims 9-12 are directed to expression cassettes comprising at least one isolated nucleotide sequence according to claim 1, as outlined above. Original claims 13-15 recite transformed cells of interest comprising a stably incorporated nucleotide sequence selected from the group of nucleotide sequences set forth in claim 1. The Examiner maintains that "the only adequately described species is a nucleic acid molecule having the nucleotide sequence set forth in SEQ ID NO:1" (see page 5, Office Action mailed August 9, 2006). Applicants respectfully disagree with the Examiner's conclusions.

Although Applicants maintain that the claims as originally filed satisfied the written description requirement, independent claims 1 and 13 have been amended to eliminate original subpart (e) directed to a nucleotide sequence that hybridizes to the complement of SEQ ID NO:1 under stringent conditions. Subparts (c) and (d) have been further amended to clarify that the

nucleotide sequences encompassed by these portions of claims 1 and 13 display at least about 90% or about 95% sequence identity *across the full length of the nucleotide sequence set forth in SEQ ID NO:1*. And finally, subpart (g) of originally filed claims 1 and 13 has been amended to expressly state that the claimed nucleotide sequences are *complementary across the full length* of at least one nucleotide sequence set forth in the other subparts of the claims. Support for the claim amendments with respect to "across the full length" of a particular sequence can be found at, for example, page 24 of the specification. The rejection under 35 U.S.C. § 112, first paragraph, will be addressed insofar as it may apply to the amended claims.

In order to satisfy the written description requirement of 35 U.S.C. § 112, the application must reasonably convey to one skilled in the art that the applicant was in possession of the claimed subject matter at the time the application was filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d (BNA) 1111, 1117 (Fed. Cir. 1991). Every species encompassed by the claimed invention, however, need not be disclosed in the specification to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. *Utter v. Hiraga*, 845 F.2d 993, 6 USPQ2d 1709 (Fed. Cir. 1988). The Federal Circuit has made it clear that sufficient written description requires simply the knowledge and level of skill in the art to permit one of skill to immediately envision the product claimed from the disclosure. *Purdue Pharm L.P. v. Faulding In.*, 230 F.3d 1320 1323, 596 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("One skilled in the art must immediately discern the limitations at issue in the claims.").

Moreover, the "Guidelines for Examination of Patent Applications Under 35 U.S.C. §112, ¶ 1, 'Written Description' Requirement" state that a genus may be described by "sufficient description of a representative number of species . . . or by disclosure of relevant, identifying characteristics , *i.e.* structure or other physical and/or chemical properties." *Id.* at 1106. This is in accordance with the standard for written description set forth in *Regents of the University of California v. Eli Lilly & Co*, 119 F.3d 1559 (Fed. Cir. 1997), where the court held that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, or chemical name' of the claimed subject matter sufficient to distinguish it from other materials." 119 F.3d at 1568, citing *Fiers v. Revel* 984 F.2d 1164 (Fed. Cir. 1993). In *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323

F.2d 926 (Fed. Cir. 2002), the Federal Circuit adopted the PTO standard for written description, stating:

> [U]nder the Guidelines, the written description requirement would be met . . . if the functional characteristics of [a genus of nucleic acids] were coupled with a disclosed correlation between that function and a structure that is sufficiently known or disclosed. We are persuaded by the Guidelines on this point and adopt the PTO's applicable standard for determining compliance with the written description requirement."

The claims of the present application meet the requirements for written description set forth by the Federal Circuit. The Examiner, however, maintains that the specification fails to provide sufficient distinguishing characteristics of the genus of claimed sequences and states that "[t]he specification does not identify any particular portion of the structure" of SEQ ID NO:1 that is characteristic of the claimed genus (page 5, Office Action mailed August 9, 2006). Contrary to the Examiner's remarks, the claims as amended recite that the nucleotide sequences encompassed by the invention are selected from the group consisting of SEQ ID NO:1, a variant of SEQ ID NO:1, wherein the variant has *Bt* toxin binding activity and at least about 90% or 95% sequence identity across the full length of SEQ ID NO:1, a nucleotide sequence that encodes the polypeptide of SEQ ID NO:2, the nucleotide sequence of the cDNA insert of the plasmid deposited with the ATCC as PTA-4935, and a nucleotide sequence complementary to the full-length nucleotide sequence of one of the above-listed sequences. Methods for determining percent identity between any two sequences are known in the art and are provided in the specification. See pages 24-29. Furthermore, the skilled artisan could readily determine nucleotide sequences that are complementary across the full length of a known sequence (e.g., SEQ ID NO:1) utilizing routine methods. Thus, the recitation of nucleotide sequences that share a particular percent identity with a specific *Bt* toxin receptor sequence (i.e., SEQ ID NO:1) or are complementary to a disclosed sequence provide very specific and defined structural parameters of the sequences that can be used in the invention. These structural limitations are sufficient to distinguish the nucleotide sequences of the invention from other nucleic acids and thus sufficiently define the genus of sequences useful in the practice of the present invention. Thus, in contrast to the Examiner's conclusions, Applicants respectfully submit that sufficient

structural information is provided to adequately support all of the nucleotide sequences encompassed by the amended claims.

Furthermore, the description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), *citing Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of nucleic acids may therefore be described by means of a recitation of a representative number of nucleotide sequences that fall within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *See Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2000). The recitation of a predictable structure (i.e., a nucleotide sequence having a specified percent identity to a particular sequence) is sufficient to satisfy the written description requirement. Thus, the application provides the structural features that characterize sequences having at least about 90% or about 95% sequence identity to SEQ ID NO:1, the recited deposited sequence, and nucleotide sequences that are complementary across the full length of SEQ ID NO:1 of one of the other claimed nucleotide sequences.

The Examiner also states that "no active variants [of the nucleotide sequence of SEQ ID NO:1] are disclosed" as evidence of lack of written description (see page 5, Office Action mailed August 9, 2006). The Examiner, however, is reminded that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2000). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2000). Here, Applicants have provided nucleotide and amino acid sequences for an exemplary novel *Bt* toxin receptor sequence and for homologous *Bt* toxin receptor sequences from *Spodoptera frugiperda* (SEQ ID NO:6), *Heliocverpa zea* (SEQ ID NO:7), *Ostrinia nubialis* (SEQ ID NO:8), *Bombyx mori* (SEQ ID NO:9), and *Manduca sexta*

(SEQ ID NO:10), which have been shown to bind to Cry1 *Bt* toxins. See pages 2-3 and Figure 2. In addition, other *Bt* toxin receptors were known in the art at the time the application was filed. Information relating to conserved regions of *Bt* toxin receptor sequences may be obtained from these sequences. A person of skill in the art would appreciate that comparison and alignment of known *Bt* toxin receptors may reveal information regarding appropriate sites or regions for modifications. By aligning these sequences, one may be able to identify conserved residues or regions within these sequences that are unlikely to tolerate mutation and still retain *Bt* toxin binding activity. Methods for aligning sequences, such as by using the CLUSTAL algorithm, are described in the specification. See pages 25-27. Thus, by reference to a standard codon table and the methods described in the specification, one of skill in the art could predict which modifications would not likely affect the biological activity of the encoded polypeptide. In light of the above remarks, Applicants respectfully disagree with the Examiner's statements that the specification (and the art) does not provide sufficient guidance regarding the structural requirements of the claimed nucleotide sequences. See, in particular, pages 4-5 of the Office Action mailed August 9, 2006. Therefore, Applicants submit that in view of the present disclosure and the knowledge and level of skill in the art the skilled artisan would readily envision the claimed invention, including the biologically active variants of SEQ ID NO:1 recited in the present claims.

An Applicant may also rely upon functional characteristics in the description, provided there is a correlation between the function and structure of the sequences recited in the claims. *Id.*, citing *Lilly* at 1568. The present claims further recite functional characteristics that distinguish the sequences of the claimed genus. Specifically, the claims recite that the variant nucleotide sequences of the invention encode polypeptides that have *Bt* toxin binding activity. The specification and the art provide standard assays that may be used to measure *Bt* toxin binding activity. See, for example, page 7. The Examiner asserts that the polypeptides encoded by the claimed nucleotide sequences are required to have *Bt* toxin binding activity but are not required to possess any particular conserved structure (see pages 4-5, Office Action mailed August 9, 2006). In contrast to the Examiner's remarks, however, the alignment of various *Bt* toxin receptors provided in Figure 2 provides structural information regarding the *Bt* toxin

binding domain, particularly the Cry1A binding domain. Thus, the recitation of variant nucleotide sequences having a specified percent identity to the *Bt* toxin receptor nucleotide sequence set forth in SEQ ID NO:1, wherein the nucleotide sequence encodes a polypeptide that has *Bt* toxin binding activity, provides very specific and defined structural parameters of the sequences that can be used in the invention and a correlation of these structural parameters with the recited functional limitation (i.e., *Bt* toxin binding activity). These structural and functional limitations are also sufficient to distinguish the nucleotide sequences of the invention from other nucleic acids and thus adequately define the genus of sequences useful in the practice of the present invention, as required by 35 U.S.C. § 112, first paragraph (written description). Accordingly, both the structural and functional properties that characterize the genus of sequences that can be used to practice the invention are specifically recited in the claims. Furthermore, the sequences that fall within the scope of the claims can be immediately envisioned by the skilled artisan and readily identified by the methods set forth in the specification.

And finally, Applicants respectfully direct the Examiner's attention to the recent Federal Circuit case *Invitrogen Corp. v. Clontech Laboratories, Inc.*, 77 USPQ2d 1161 (Fed. Cir. 2005). The claims in the *Invitrogen* case were broadly drawn to an isolated polypeptide having DNA polymerase activity and substantially reduced RNase H activity, wherein the polypeptide is encoded by a modified reverse transcriptase nucleotide sequence. The Court distinguished the cases of *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), and *Fiers v. Revel*, 25 USPQ2d 1601 (Fed. Cir. 1993), from the facts of *Invitrogen* stating that "[i]n those cases, the patent specifications at issue did not identify the sequence (structure) of *any* embodiment of DNA claimed therein." *Invitrogen Corp.* 77 USPQ2d at 1175-76 (emphasis added). The Court further distinguished the two previous cases, stating:

> [T]he shared written description for the patents-in-issue [in the *Invitrogen* case] recites both the DNA and amino acid sequences of a representative embodiment of the claimed RT enzyme. The specification also discloses test data that the enzyme produced by the listed sequence has the claimed features -- DNA polymerase activity without RNase activity. Under both the *Eli Lilly* and *Fiers* analysis, the specification at bar is sufficient. *Id.* at 1176 (emphasis added).

Similarly, as discussed above, the present specification discloses a representative embodiment of the claimed *Bt* toxin receptor sequences (i.e., SEQ ID NO:1) and further describes that the nucleotide sequence set forth in SEQ ID NO:1 has the claimed feature, namely *Bt* toxin binding activity. The amended claims are directed to a nucleotide sequence expressly disclosed within the application, functional variants having a specified percent identity to the full length of disclosed sequence (i.e., SEQ ID NO:1), a nucleotide sequence that encodes the polypeptide of SEQ ID NO:2, an ATCC deposited nucleotide sequence, and nucleotide sequences complementary to the full-length sequence of any of the above-referenced nucleotide sequences. Therefore, under the holdings of *Invitrogen*, *Lilly*, and *Fiers*, the amended claims are adequately supported by the written description.

In view of the above remarks and claim amendments, Applicants submit that the relevant identifying structural and functional properties of the genus of nucleotide sequences encompassed by the present claims would be clearly recognized by one of skill in the art, and, therefore, the full breadth of the claims is supported by the specification. Consequently, Applicants were in possession of the invention at the time the application was filed, and the rejection of the claims under 35 U.S.C. § 112, first paragraph, for lack of written description should be withdrawn.

The Rejection of the Claims Under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn

Claims 1-3 and 9-15 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed.

With respect to claim 1, the Examiner has indicated that the claim term "*Bt* toxin" must be fully spelled out in the first instance of use. In accordance with the Examiner's recommendation, subpart (c) of claim 1 has been amended to recite "*Bacillus thuringiensis* (*Bt*) toxin."

The Examiner has further indicated that it is unclear from the language of claim 1 (specifically current subpart (f)) the portion of the claimed nucleotide sequence which is

complementary to a nucleotide sequence recited in subparts (a) – (e). To expedite prosecution, claims 1 and 13 have been amended to expressly state "a nucleotide sequence complementary across the full length of at least one nucleotide sequence set forth in a), b), c), d), or e)."

In view of the claim amendments, claims 1-3 and 9-15 particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Accordingly, the rejection of the claims under 35 U.S.C. § 112, second paragraph, should be withdrawn.

The Rejection of the Claims Under 35 U.S.C. § 101 Should Be Withdrawn

Claims 9-15 were rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. This rejection is respectfully traversed.

Claims 9-12 are directed to expression cassettes comprising at least one isolated nucleotide sequence according to claim 1. Claims 13-15 recite transformed cells having stably incorporated within their genome a nucleotide sequence of claim 1. The Examiner maintains that claims 9-15 do not constitute patentable subject because "the claims do not sufficiently distinguish over cells [or expression cassettes] that exist naturally" absent express recitation of "isolated and purified" in the claims (see page 7, Office Action mailed August 9, 2006). While the Examiner is correct that naturally occurring products are not patentable under 35 U.S.C. § 101, Applicants respectfully disagree with the Examiner's assessment of claims 9-15.

The Examiner has cited, among other cases, *Diamond v. Chakrabarty*, 447 US 303, 206 USPQ 193 (U.S. 1980) as evidence that the subject matter of claims 9-15 is unpatentable. The U.S. Supreme Court held in that case, however, that a genetically engineered microorganism was statutory subject matter and eligible for patent protection. The Court further explained that the patent system is directed to the "inventive works of mankind" and that Congress intended that the patent laws should be given wide scope with respect to statutory subject matter. *Id.*

The claims at issue here clearly fall within the "inventive works" contemplated by the U.S. Supreme Court in *Diamond*. First of all, claim 9 and all claims dependent thereon recite an expression cassette comprising at least one nucleotide sequence according to claim 1 operably linked to a promoter that drives expression in a cell. The language of claim 1 expressly states

that the claimed nucleotide sequences are "isolated" (i.e., not merely found in nature). Accordingly, an expression cassette comprising an isolated nucleotide sequence operably linked to a promoter necessarily requires that the claimed expression cassettes are engineered and are therefore not naturally occurring. Moreover, the Examiner's attention is drawn to pages 9-12 of the present specification which further indicate that the expression cassettes of the invention do not read on nature. Therefore, contrary to the Examiner's conclusions, Applicants respectfully submit that claims 9-12, as written, are directed to statutory subject matter.

Furthermore, claims 13-15 recite "transformed cells" that comprise a stably incorporated nucleotide sequence of the invention. As would be appreciated by a person of skill in the art of molecular biology, the term "transformed" inherently indicates that the cells have been manipulated or recombinantly engineered to introduce a nucleotide sequence of interest into the cell such that they could not be classified as "naturally occurring" within the meaning of 35 U.S.C. § 101 or under the holding of *Diamond*. Accordingly, claims 13-15 are also directed to statutory subject matter.

In view of the above remarks, Applicants respectfully request that the rejection of claims 9-15 under 35 U.S.C. § 101 be withdrawn.

The Rejection of the Claims Under 35 U.S.C. § 102 Should Be Withdrawn

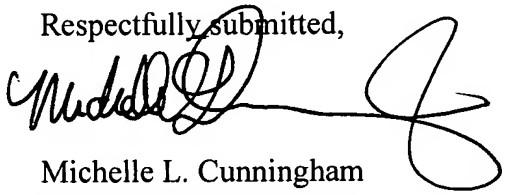
Claims 1 and 9-15 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 7,029,851 (hereinafter "the '851 patent"). This rejection is respectfully traversed.

The '851 patent is directed to nucleic acid probes that specifically identify a gene for *Bt* toxin resistance in insect populations. The Examiner asserts that the cited reference anticipates claims 1 and 9-15 because the nucleotide sequence of SEQ ID NO:1 of the '851 patent possesses a region that is complementary to a short section of SEQ ID NO:1 of the present invention. Specifically, nucleotide residues 5-11 of SEQ ID NO:1 of the '851 patent are complementary to nucleotide residues 214 to 220 of SEQ ID NO:1 of the present invention. As described above, the claims have been amended to expedite prosecution and now no longer recite nucleotide sequences that hybridize to a complement of SEQ ID NO:1. Moreover, the claims have been

further amended to indicate that the claimed nucleotide sequences are complementary "across the full length" of a sequence recited in claims 1 or 13. Therefore, the '851 patent does not teach each and every element of the amended claims, and the rejection under 35 U.S.C. § 102(e) should be withdrawn.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



Michelle L. Cunningham
Registration No. 51,072

Customer No. 29122
ALSTON & BIRD LLP
Bank of America Plaza
101 South Tryon Street, Suite 4000
Charlotte, NC 28280-4000
Tel Raleigh Office (919) 862-2200
Fax Raleigh Office (919) 862-2260

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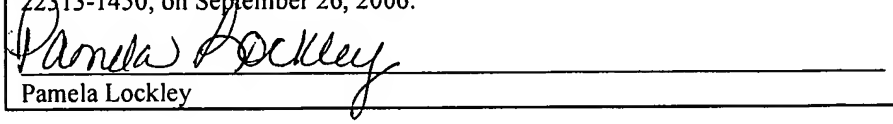

Pamela Lockley

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Amendments to the Drawings:

Please replace originally filed Figure 2 with the substitute figure submitted herewith. Figure 2 has been amended as the highlighted portions of the originally filed drawing were too dark to be legible.